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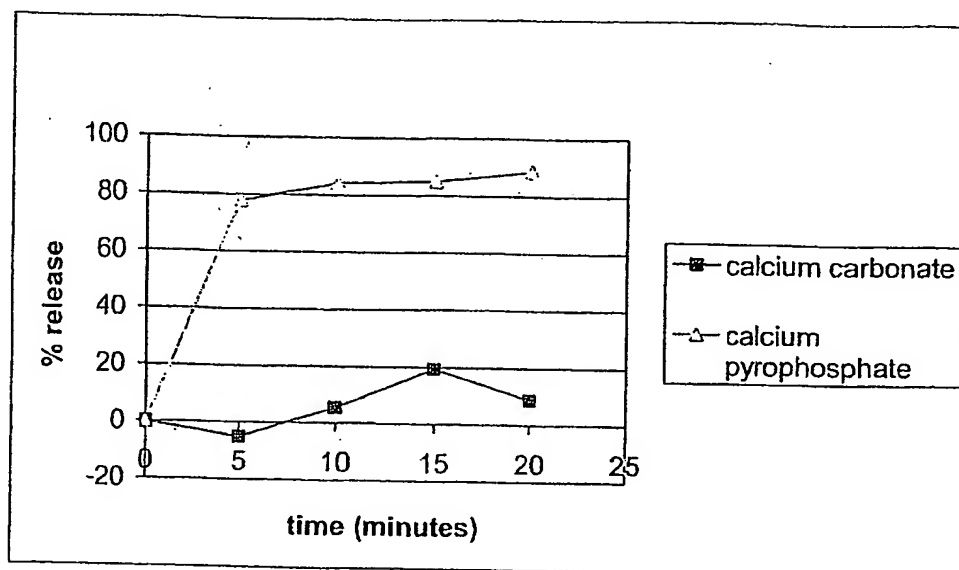
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ance Notes on Codes and Abbreviations" appearing at the begin-
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(54) Title: A SOLID ORAL TOOTH WHITENING COMPOSITION



(57) Abstract: The present invention provides a solid, oral tooth whitening composition comprising a tooth whitening agent com-
prising calcium pyrophosphate present in an amount between 0.5% and 9% by weight of the composition, excluding any coating. In
one embodiment, the composition of the invention comprises an additional tooth whitening agent

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Title: A solid oral tooth whitening composition

Technical Field

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The invention relates to solid, oral tooth whitening compositions. The invention further relates to the use of such compositions to whiten tooth surfaces.

Background Art

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Tooth whitening or stain removing agents are known to be added to dentifrice compositions such as toothpaste, mouthwash, chewing gum, confectionary compositions and the like. The use of such compositions for reducing stains and discolouration of tooth surfaces thereby improving the general cosmetic appearance of the teeth is likewise well-known. Teeth with extrinsic stains are objectionable both on the basis of cosmetic appearance and also socially as indication of poor oral hygiene.

15

Some products contain peroxides, but these are, however, problematic from a toxicological point of view. Another approach to tooth whitening products is to add abrasives - known mainly from dentifrices. Not all of these are legal in confectionary.

20

Several abrasive agents have been used for tooth whitening purposes and these are known to the person skilled in the art. Examples of abrasive agents include calcium carbonate, sodium bicarbonate, sodium metaphosphate, potassium metaphosphate, tricalcium phosphate, dihydrated dicalcium phosphate, bentonite, zirconium silicate

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or other siliceous materials. Other suitable abrasives are described in U.S. Patent No. 4,170,633 and U.S. Patent No. 4,891,211, incorporated herein by reference.

Several patents and patent applications disclose the use of abrasive materials in solid, oral compositions, see for example U.S. Patent Nos. 5,147,632 and 5,496,541, EP Patent No. 372,603, International Publication Nos. WO 02/19834 and WO 01/56399.

US Patent Application US 2002/0142068 discloses chewing gum formulations including sodium pyrophosphate and encapsulated aspartame.

US Patent No. 4,233,288 discloses a gum emulsified liquid composition for delivering and preserving the liquid content in the mouth. The herein disclosed examples describe a gum emulsified liquid composition comprising 5% of calcium pyrophosphate and more than 50% of liquid components.

U.S. Patent No. 3,590,120 discloses a chewing gum comprising a polishing agent comprising a mixture of fine and coarse zirconium silicate particles. Disclosed herein are reference chewing gum compositions containing 10% of calcium pyrophosphate or 10% of calcium carbonate, respectively. The cleaning/polishing effects of said compositions are shown to decrease in the order $ZrSiO_4$, $CaCO_3$ and CaP_2O_7 . Indicative studies have however shown some problematic toxicological properties of zirconium silicate (Elmore AR, Cosmetic Ingredient Review Expert Panel, Final report on the safety assessment of aluminum silicate, calcium silicate, magnesium aluminium silicate, magnesium silicate, magnesium trisilicate, sodium

aluminium silicate, magnesium silicate, magnesium trisilicate, sodium magnesium silicate, zirconium silicate, attapulgite, bentonite, Fuller's earth, hectorite, kaolin, lithium magnesium silicate, lithium magnesium sodium silicate, montmorillonite, pyrophyllite, and zeolite, Int. J Toxicol. 2003; 22 Suppl. 1:37-102) and the use of
5 zirconium compounds in solid oral compositions is prohibited in a number of countries.

Thus, a need exists in the art to identify and use abrasives in a solid, oral tooth whitening composition to obtain an increased whitening effect.

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Disclosure of Invention

The present invention relates to a solid, oral tooth whitening composition comprising more than 75% by weight of solid materials, said composition comprising:

15

- (a) a chewing gum or confectionary base,
- (b) conventional chewing gum or confectionary additives,
- (c) a tooth whitening agent comprising calcium pyrophosphate present in an amount of 0.5 to 9% by weight of the composition.

20

Furthermore, the present invention relates to the use of a composition according to the present invention to whiten tooth surfaces.

Furthermore, the present invention relates to a method of whitening tooth surfaces.

Brief Description of the Drawings

The invention is explained in detail below with reference to the drawing(s), in which
5 Fig. 1 shows the release percentage as a function of time for calcium carbonate and calcium pyrophosphate, respectively, present in a chewing gum composition.

Best Modes for Carrying out the Invention

10 It has now surprisingly been demonstrated, using *in vitro* tests, that improved stain removal and stain inhibition effects of solid, oral compositions can be achieved using from 0.5 to 9 % of calcium pyrophosphate as an abrasive agent, compared to the use of the often used abrasive, calcium carbonate. These effects are unexpected, seen
15 in the light of the results presented in US 3,590,120, in which the polishing effect of CaP_2O_7 was significantly poorer than that of CaCO_3 .

In addition to these results, it has also been surprisingly shown, using *in vivo* tests, that calcium pyrophosphate-containing chewing gum results in an improved removal
20 of stain on tooth surfaces which do not normally come into contact with the gum while chewing, i.e. maxillary facial tooth surfaces, as well as on tooth surfaces on which stains build up rapidly and heavily and is the most difficult to remove, i.e. proximal tooth surfaces.

25 Typically, solid, oral tooth whitening compositions are intended to comprise a recommended daily dose of tooth whitening agent of about 40 to 700 mg. Conven-

iently, this dose may be divided into multiple sub-doses, such as 8 units of the composition, each unit weighing approximately 900-1000 mg, excluding any coating. Thus, a content of 0.5% to 9 % of tooth whitening agent corresponds to a composition unit content of approximately 4.5 to 90 mg of tooth whitening agent.

5

The compositions of the invention are essentially solid and comprise more than 75%, preferably more than 85%, even more preferably more than 95%, by weight of the composition of solid materials.

10 In a preferred embodiment of the invention, calcium pyrophosphate is present in an amount of between 3% and 8%, preferably between 4.5% and 7.5 %, even more preferably between 5.5% and 7 %, by weight of the composition, respectively, excluding any coating.

15 In one embodiment, the composition according to the invention may be formulated as a chewing gum composition, said chewing gum composition preferably comprising a gum base constituting from 10% to 99%, particularly from 15% to 80%, preferably 25% to 60 % by weight of the composition. As used herein the expression "gum base" refers in general to the water insoluble part of the chewing gum. Chew-
20 ing gum base formulations typically comprise one or more elastomeric compounds which may be of synthetic or natural origin, one or more resin compounds which may be of synthetic or natural origin, fillers, softening compounds and minor amounts of miscellaneous ingredients such as antioxidants and colorants, etc.

6.

- In this context, useful synthetic elastomers include, but are not limited to, synthetic elastomers listed in Food and Drug Administration, CFR, Title 21, Section 172.615, the Masticatory Substances, Synthetic) such as polyisobutylene with a gas pressure chromatography (GPC) average molecular weight in the range of about 10,000 to about 1,000,000 including the range of 50,000 to 80,000, isobutylene-isoprene copolymer (butyl elastomer), styrene-butadiene copolymers e.g. having styrene-butadiene ratios of about 1:3 to about 3: 1, polyisoprene, polyethylene, vinyl acetate-vinyl laurate copolymer e.g. having a vinyl laurate content of about 5 to about 50% by weight such as 10 to 45% by weight of the copolymer, and combinations hereof.
- Useful natural non-degradable elastomers include the elastomers listed in Food and Drug Administration, CFR, Title 21, Section 172.615, as "Masticatory Substances of Natural Vegetable Origin" including natural rubber compounds such as smoked or liquid latex and guayule and other natural gums including jelutong, lechi caspi, massaranduba balata, sorva, perillo, rosindinha, massaranduba chocolate, chicle, nispero, gutta hang kang, and combinations thereof. The preferred synthetic elastomer and natural elastomer concentrations vary depending on whether the chewing gum in which the base is used is adhesive or conventional, bubble gum or regular gum. Presently preferred natural elastomers include jelutong, chicle, massaranduba balata and sorva.

20

Resin in conventional chewing gum bases typically include synthetic resins such as poly(vinyl acetate) (PVAc) and natural resins such as rosin esters which are often referred to as ester gums. Additionally, natural resins such as glycerol esters of partially hydrogenated rosins, glycerol esters of polymerised rosins, glycerol esters of

partially dimerised rosins, glycerol esters of tally oil rosins, pentaerythritol esters of partially hydrogenated rosins, methyl esters of rosins, partially hydrogenated methyl esters of rosins and pentaerythritol esters of rosins are typically applied in chewing gum bases. Other resinous compounds typically applied in chewing gum bases include synthetic resins such as terpene resins derived from alpha-pinene, beta-pinene, and/or d-limonene and natural terpene resins.

A chewing gum base formulation may, if desired, include one or more fillers/texturisers including as examples, magnesium and calcium carbonate, sodium sulphate, ground limestone, silicate compounds such as magnesium and aluminium silicate, kaolin and clay, aluminium oxide, silicon oxide, talc, titanium oxide, mono-, di- and tri-calcium phosphates, cellulose polymers, such as wood, and combinations thereof.

A gum base formulation may, in accordance with the present invention comprise one or more softening agents e.g. sucrose polyesters including those disclosed in WO 00/25598, which is incorporated herein by reference, tallow, hydrogenated tallow, hydrogenated and partially hydrogenated vegetable oils, cocoa butter, glycerol monostearate, glycerol triacetate, lecithin, mono-, di- and triglycerides, acetylated monoglycerides, fatty acids (e.g. stearic, palmitic, oleic and linoleic acids), and combinations thereof. As used herein the term "softener" designates an ingredient, which softens the gum base or chewing gum formulation and encompasses waxes, fats, oils, emulsifiers, surfactants and solubilisers.

To soften the gum base further and to provide it with water binding properties, which confer to the gum base a pleasant smooth surface and reduce its adhesive properties, one or more emulsifiers is/are usually added to the composition, typically in an amount of 0 to 18% by weight, preferably 0 to 12% by weight of the gum base.

- 5 Mono- and diglycerides of edible fatty acids, lactic acid esters and acetic acid esters of mono- and diglycerides of edible fatty acids, acetylated mono and diglycerides, sugar esters of edible fatty acids, Na-, K-, Mg- and Ca-stearates, lecithin, hydroxylated lecithin and the like are examples of conventionally used emulsifiers which can be added to the chewing gum base. In case of the presence of a biologically or
- 10 pharmaceutically active ingredient as defined below, the formulation may comprise certain specific emulsifiers and/or solubilisers in order to disperse and release the active ingredient.

- Waxes and fats are conventionally used for the adjustment of the consistency and for
- 15 softening of the chewing gum base when preparing chewing gum bases. In connection with the present invention any conventionally used and suitable type of wax and fat may be used, such as for instance rice bran wax, polyethylene wax, petroleum wax (refined paraffin and microcrystalline wax), paraffin, bees' wax, carnauba wax, candelilla wax, cocoa butter, degreased cocoa powder and any suitable oil or fat, as
- 20 e.g. completely or partially hydrogenated vegetable oils or completely or partially hydrogenated animal fats.

In one embodiment the gum base is wax-free.

Furthermore, the gum base formulation may, in accordance with the present invention, comprise colourants and whiteners such as FD&C-type dyes and lakes, fruit and vegetable extracts, titanium dioxide and combinations thereof. Further useful chewing gum base components include antioxidants, e.g. butylated hydroxytoluene (BHT), butyl hydroxyanisol (BHA), propylgallate and tocopherols, and preservatives.

The composition of chewing gum base formulations which are admixed with chewing gum additives as defined below can vary substantially depending on the particular product to be prepared and on the desired masticatory and other sensory characteristics of the final product. However, typical ranges (weight%) of the above gum base components are: 5 to 50% by weight elastomeric compounds, 5 to 55% by weight elastomer plasticizers, 0 to 50% by weight filler/texturiser, 5 to 35% by weight softener and 0 to 1% by weight of miscellaneous ingredients such as antioxidants, colorants, etc.

Chewing gum compositions may be formulated as sticks or pellets, and may be coated with a suitable coating. Concentrations given throughout this disclosure are based on weight excluding coating unless specifically indicated.

20

In another embodiment, the compositions of the invention are formulated as confectionary compositions comprising a confectionary base, said confectionary base preferably comprising from 0% to 99%, particularly from 15% to 98%, preferably 30% to 97% by weight of the composition. Non-limiting examples of confectionary com-

positions according to the invention include high boiling, grained sugar confection-
ary, chocolate, compressed tablets, gummy confectionary and jellies.

In addition to the ingredients listed above, the compositions comprised by the pre-
5 sent invention may also contain one or more conventional additives such as sweet-
eners, high intensity sweeteners, taste enhancers, flavouring agents and the like.
Sweeteners, high intensity sweeteners and taste enhancers are well known to the
skilled person. Non-limiting examples of sweeteners comprise sugar sweeteners in-
cluding saccharides such as sucrose, dextrose, glucose, maltose, dextrans, D-
10 tagatose, trehalose, dried invert sugar, fructose, levulose, galactose, corn syrup sol-
ids, and the like, alone or in combination. Other examples of sweeteners comprise
sugarless sweeteners including polyhydric alcohols such as sorbitol, mannitol, xylitol,
glycerol, hydrogenated starch hydrolysates, maltitol, isomaltitol, erythritol, lacti-
tol and the like, alone or in combination. Sugarless sweeteners are preferred.

15

Preferred high intensity sweeteners include but are not limited to sucralose, aspar-
tame, salts of acesulfame, alitame, saccharin or salts thereof, neotame, cyclamic acid
and salts thereof, glycyrrhizin, dihydrochalcones, thaumatin, monnelin, sterioside
and the like, alone or in combination.

20

A variety of flavours known in the art may be used, such as cinnamon, wintergreen,
eucalyptus, spearmint, peppermint, menthol, anise as well as fruit flavours such as
apple, pear, peach, strawberry, cherry, apricot, orange, watermelon, banana and the
like; bean-derived flavours, such as coffee, cocoa and the like. Flavouring agents are

incorporated in the chewing gum formulation at a concentration of about 0.5 to about 5 % by weight and preferably 1 to 3 % by weight.

The compositions of the invention may or may not contain sugar. Sugar-free
5 compositions, however, are preferred.

It may be advantageous to include one or more additional tooth whitening agents. Examples of such additional tooth whitening agents are well known in the art and include abrasives as well as bleaching agents. Abrasive materials comprise as non-
10 limiting examples silica, alumina, calcium carbonate, dicalcium phosphate, hydroxyapatite, trimetaphosphates and insoluble hexametaphosphates. Bleaching agents comprise agents such as peroxy compounds, e.g. potassium peroxydiphosphate and urea-peroxid. Effervescing systems such as sodium bicarbonate, alone or in combination with citric acid as well as colour change systems may also be incor-
15 porated into compositions comprised by the present invention.

In chewable oral compositions, said additional whitening agents are usually present in between 0.01% and 10.0%, preferably between 0.1 and 2.0%, more preferably between 0.25% and 1.0% by weight of the composition, excluding any coating.

20

A preferred additional tooth whitening agent comprises a bicarbonate salt. In one embodiment, said bicarbonate salt comprises sodium bicarbonate in an amount of between 0.3% and 0.4% by weight of the compositions excluding any coating.

A range of active agents may be added to the compositions of the invention. Such agents may comprise one or more of the following; oral hygiene promoting agents, anti-calculus agents, anti-microbial agents, anti-inflammatory agents, desensitising agents, therapeutically active agents, remineralising agents. Non-limiting examples

5 comprise anti-carries agents such as sodium, calcium, magnesium and stannous fluoride, amine fluorides, disodium monofluorophosphate, sodium trimetaphosphate and casein; antimicrobial agents, e.g. Triclosan, chlorhexidine, copper, zinc and stannous salts such as zinc citrate, zinc sulphate, zinc glycinate, sodium zinc citrate and stannous pyrophosphate, sanguinarine extract, metronidazole, quaternary ammonium

10 compounds, such as cetylpyridinium chloride; bis-guanides, such as chlorhexidine digluconate, hexetidine, octenidine, alexidine; and halogenated bisphenolic compounds, such as 2,2' methylenebis-(4-chloro-6-bromophenol); anti-inflammatory agents such as ibuprofen, flurbiprofen, aspirin, indomethacin etc.; plaque acid buffers such as urea, calcium lactate, calcium glycerophosphate and strontium polyacry-

15 lates; desensitising agents, e.g. potassium citrate, potassium chloride, potassium tartrate, potassium bicarbonate, potassium oxalate, potassium nitrate and strontium salts; anti-calculus agents, e.g. hypophosphite-containing polymers, organic phosphonates and phosphocitrates etc.; gum protection agents, e.g. vegetable oils such as sunflower oil, rape seed oil, soybean oil, safflower oil; silicone oil; and hydrocarbon

20 oil; pharmaceutically acceptable carriers, e.g. starch, sucrose, water or water/alcohol systems etc.; surfactants, such as anionic, nonionic, cationic and zwitterionic or amphoteric surfactants. Other agents which may be incorporated in the chewable compositions of the present invention are agents to counter breath malodour and include water soluble zinc salts (at least 1% soluble) particularly zinc chloride, zinc acetate,

zinc citrate and zinc gluconate.

The additives, the whitening agents and the optional active agents comprised by the present invention may be encapsulated. This may be done in order to achieve a slow
5 release of the encapsulated agents upon entering the oral environment. For example, a longer lasting sweetening of the compounds comprised by the present invention may be achieved by encapsulating the sweetening agents. A longer release time of the whitening agents as well as any therapeutic compound may likewise be achieved.

10

Another advantage of encapsulating the agents comprised by the invention may be to obtain an increased stability of the agents, thus lending a longer storage life at a greater range of storage conditions to the compositions of the invention.

15 Any standard method giving partial or full encapsulation can be used for encapsulation. Suitable methods include, but are not limited to, spray drying, spray chilling, fluid-bed coating, and coacervation. These methods can be used individually or in any combination in a single step process or multiple step process.

20 Generally, compositions of high organic solubility, good film forming properties, and low water solubility, provide a suitable encapsulation. These compositions include acrylic polymers and copolymers, carboxyvinyl polymers, polyamides, polystyrene, polyvinyl acetate, polyvinyl acetate phthalate, polyvinyl pyrrolidone, and waxes.

However, only food grade materials should be used for the encapsulation. Two standard food grade coating materials, which are good formers, but not water soluble, are shellac and Zein. Others which are more water soluble, but also good film formers, are materials such as agar, alginates, a wide range of cellulose derivatives like ethyl cellulose and hydroxypropylmethyl cellulose, dextrin, gelatin and modified starches. It is also possible to use other encapsulants like acacia or maltodextrin for encapsulation.

10 In yet another embodiment of the invention, it may be desirable to include a supplement, such as vitamins and/or minerals in the composition according to the invention. Vitamins are preferably added in concentrations of between 10 % - 100% of the recommended daily allowance (RDA).

15 Especially vitamin C may be added to the compositions of the invention.

It may be desirable to include urea in the compositions of the invention. Urea may be added as a plaque acid neutralising agent. Usually urea is added to chewable compositions in between 0.15% and 25%, particularly between 0.4% and 10%, preferably between 0.8% and 5.0%, even more preferably between 1.5 % and 2.5% by weight.

In another embodiment, the present invention relates to the use of the compositions of the invention to whiten tooth surfaces and/or prevent discolouration of tooth sur-

faces. Especially, the compositions of the invention may be used to remove or prevent discolouration of teeth due to the use of tobacco-related products and/or coffee-related products.

5 Examples

In the following examples 1-4, the compositions are based on a standard chewing gum composition in addition to the specified ingredients. The standard chewing gum composition used herein consists essentially of the following ingredients:

10

Gum base	29.64%
Sweeteners	60.98%
High intensity sweeteners	0.12%
Flavours	1.80%
15 Buffers/stabilizer	2.28%
Softeners	0.07%
Colourants	0.35%

Example 1

20 The effect of chewing gum on the removal of extrinsic stains from teeth after 120 minutes

Three standard chewing gum compositions containing, by weight of the core composition, i.e. excluding coating, 4.5% of calcium carbonate, 4.5% of calcium pyrophosphate and 6.5% of calcium pyrophosphate, respectively, were assayed for the
25 effect on the removal of extrinsic stains on tooth surfaces.

The experiments were conducted using a modification of the laboratory method de-

scribed by Stookey, GK; Burkhardt, T.A; and Schemehorn, B.R; In vitro removal of stain with dentifrices, J Dent Res 61(11):1236-1239, Nov 1982, which has been shown to correlate with the cleaning/whitening properties of dentifrices in clinical trials. The general experimental design consists of the use of a specially designed mechanical mastication device to treat stained teeth with the test chewing gums (Kleber, CJ; Schimmele RG, Putt, MS, Muhler JC: A mastication device designed for the evaluation of chewing gums, J Dent Res 60: 109-114, 1981). The amount of stain on the teeth before and after treatment is measured quantitatively using a colorimeter.

10

Each composition was tested on eight enamel pieces. The mean values and the standard deviations are shown in column 2 (ΔE). The maximum removal and the concomitant standard deviation are shown in column 3 (maximum ΔE). The % of the reduction of stains is shown in column 4 (Reduction).

15

The values in each column with the same superscript are not statistically different, while those with different superscript are different at $p < 0.05$ based on ANOVA and SNK testing.

Table 1

Whitening agent	ΔE	maximum ΔE	Reduction
4.5% CaCO_3	3.00 (1.12 ^a)	27.79 (2.33 ^a)	10.8% ^a
4.5% CaP_2O_7	5.71 (1.93 ^b)	27.04 (2.13 ^{a,b})	21.1% ^b
6.5% CaP_2O_7	8.05 (2.76 ^c)	26.18 (2.29 ^{a,c})	30.4% ^c

20

Example 2The effect of chewing gum on the inhibition of extrinsic stain formation

The chewing gum compositions disclosed in Example 1 were assayed for the effect
5 on the inhibition of extrinsic stain formation on tooth surfaces.

The experiments were conducted using a special laboratory method that has been developed to determine the potential of chewing gum to inhibit the formation of dental stains and maintain white teeth. This method is based on a model that is used
10 to evaluate the tooth whitening properties of toothpastes and is predictive of findings in human clinical studies. The general experimental design consists of the use of a specially designed mechanical mastication device to treat teeth with chewing gum while they undergo a daily staining process (Kleber, CJ; Schimmele RG, Putt, MS, Muhler JC: A mastication device designed for the evaluation of chewing gums, J
15 Dent Res 60: 109-114). The amount of stain which accumulates on the teeth is measured quantitatively using a colorimeter.

The mean values and the standard deviations are shown in column 3 (ΔE). The maximum removal value is shown in column 4 (maximum ΔE).

20

The values in each column with the same superscript are not statistically different, while those with different superscript are different at $p < 0.05$ based on ANOVA and SNK testing.

Table 2

Treatment		Stain formation scores	
Whitening agent	Time (days)	ΔE	maximum ΔE
4.5% CaCO_3	7	$19.99 \pm 1.91^{a,b}$	8.9 %
4.5% CaP_2O_7	7	$17.96 \pm 2.31^{b,c}$	18.1 %
6.5% CaP_2O_7	7	16.23 ± 2.39^c	26.0 %
Water	7	21.94 ± 1.75^a	—
4.5% CaCO_3	10	22.99 ± 1.03^a	8.3 %
4.5% CaP_2O_7	10	21.63 ± 1.94^a	13.7 %
6.5% CaP_2O_7	10	19.38 ± 1.90^b	22.7 %
Water	10	25.06 ± 1.60^c	—
4.5% CaCO_3	14	24.44 ± 1.33^a	7.7 %
4.5% CaP_2O_7	14	22.87 ± 1.72^a	13.6 %
6.5% CaP_2O_7	14	20.53 ± 1.59^b	22.5 %
Water	14	26.48 ± 1.69^c	—

Example 3The effect of tooth whitening chewing gum on stain removal

Standard chewing gum compositions were assayed for the effect on the removal of stains on tooth surfaces, said compositions containing, by weight of the core, excluding any coating, 6.5% of calcium pyrophosphate and 0.38% of sodium bicarbonate, 4.5% of calcium carbonate and 0.38% of sodium bicarbonate, 0.38% of sodium bicarbonate and a no gum control, respectively.

- 10 A group of test persons were divided into four test groups and instructed to chew 2 pieces of chewing gum compositions as specified above, 4 times per day, each for 15 minutes, and allowed one brush per day (morning) with an assigned brush and

dentrifrice. The test persons were then examined by persons skilled in the art using the modified lobene stain index (MLSI), well known to the person skilled in the art.

The results of the total MLSI scores are shown in Table 3, wherein N = the number of subjects in the group, baseline (column 3) shows the MLSI score prior to the treatment, week 4 and week 8 show the total MLSI score (covariate adjusted, baseline 3.77) after 4 weeks and 8 weeks of treatment, respectively.

The values with the identical superscript letters are not statistically different, while those with different superscript are different at $p < 0.05$ (2-tail test).

Table 3

Whitening agent	N	Baseline	Week 4	Week 8
6.5% CaP ₂ O ₇ + 0.38% NaHCO ₃	49	3.83 ± 1.32	2.45 ± 0.13 ^a	2.05 ± 0.14 ^a
4.5% CaCO ₃ + 0.38% NaHCO ₃	53	3.66 ± 1.28	2.56 ± 0.13 ^a	2.31 ± 0.13 ^{a,b}
0.38% NaHCO ₃	52	3.89 ± 1.24	2.71 ± 0.13 ^a	2.46 ± 0.13 ^b
No gum control	54	3.69 ± 1.35	2.65 ± 0.13 ^a	2.45 ± 0.13 ^b

Tables 4 and 5 show the results from the above mentioned clinical trials in per cent of stains removed after 8 weeks of treatment presented for different areas of the teeth. The total (column 3) shows the total removal of stains whereas the remaining columns specify the percentage of removed stain on specific teeth areas. The stain reduction scores for the chewing gum groups were calculated vs. the no gum control group.

* = statistically different from the control group at $p < 0.05$. Number of subjects (N)

in each group as above.

Table 4

% Reduction in stain

Whitening agent	N	Total	Maxilla	Man- dible	Facial	Lingual	Margi- nal	Body	Pro- ximal
6.5% CaP_2O_7 + 0.38% NaHCO_3	49	16*	26*	12	17	16*	11	29*	16*
4.5% CaCO_3 + 0.38% NaHCO_3	53	6	17	0	4	6	6	7	5
0.38% NaHCO_3	52	0	2	-2	1	-1	-8	1	1
No gum control	54	---	---	---	---	---	---	---	---

Table 5

% Reduction in stain

Whitening agent	N	Total	Maxilla/ Facial	Mandible/ Facial	Maxilla/ Lingual	Mandible/ Lingual
6.5% CaP_2O_7 + 0.38% NaHCO_3	49	16*	36*	11	22*	11
4.5% CaCO_3 + 0.38% NaHCO_3	53	6	22	-4	13	3
0.38% NaHCO_3	52	0	19	-6	-5	2
No gum control	54	---	---	---	---	---

- 5 Table 6 shows the results from the above mentioned clinical trials on the effect of tooth whitening chewing gum on the stain removal from the teeth of smokers in total MLSI scores (covariate adjusted, baseline = 3.86).

Table 6

Whitening agent	N	Baseline	Week 4	Week 8
6.5% CaP_2O_7 + 0.38% NaHCO_3	11	4.06 ± 1.22	2.71 ± 0.33^a	2.01 ± 0.34^a
4.5% CaCO_3 + 0.38% NaHCO_3	11	3.95 ± 0.98	2.89 ± 0.33^a	$2.63 \pm 0.34^{a,b}$
0.38% NaHCO_3	17	3.85 ± 1.18	3.12 ± 0.26^a	3.09 ± 0.27^b
No gum control	15	3.65 ± 1.43	2.73 ± 0.28^a	$2.52 \pm 0.29^{a,b}$

Example 4

Two standard chewing gum compositions containing 1.61 g Ca/100 g and 1.27 g Ca/100 g in the form of calcium carbonate and calcium pyrophosphate, respectively, were assayed for the degree of release of their calcium source upon chewing. These concentrations are by weight of the core excluding any coating, approximately 4.5% of calcium carbonate and 6.5% of calcium pyrophosphate.

2 test persons each chewed one piece of chewing gum containing calcium carbonate and one piece of chewing gum containing calcium pyrophosphate for 0, 5, 10, and 20 minutes, respectively. The amount of calcium in the gum residue was determined by extraction in a binary mixture of chloroform and 1% hydrochloric acid (HCl) water phase. The water phase was subsequently analyzed by atomic absorption spectroscopy (AAS). The release percentage was calculated as:

$$\% \text{ Release} = 100\% - C_T * 100\% / C_{T0}$$

Where C_T = concentration to time T minutes, and C_{T0} = concentration to time $T_0 = 0$ minutes.

The result is shown in Fig. 1. It is shown that within 5 minutes more than 80% of calcium pyrophosphate is released from the composition whereas less than 20% of calcium carbonate is released after more than 15 min. of chewing the two otherwise
5 identical chewing gum compositions.

Example 5

This non-limiting example discloses the inventive composition formulated as a confectionary composition, wherein the sweeteners constitute the confectionary base.

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The composition is based on a standard confectionary composition in addition to the specified tooth whitening agent comprising calcium pyrophosphate. The standard confectionary composition used herein consists essentially of the following ingredients:

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Sweeteners	97.49%
High intensity sweeteners	0.13%
Flavours	0.18%
Sodium bicarbonate	0.12%
20 Calcium pyrophosphate	2.08%

Claims

1. A solid, oral tooth whitening composition comprising more than 75% by weight of solid materials, said composition comprising:

5

- (a) a chewing gum or confectionary base,
- (b) conventional chewing gum or confectionary additives,
- (c) a tooth whitening agent comprising calcium pyrophosphate present in an amount of between 0.5% and 9% by weight of the composition, excluding any coating

10 compositions.

2. The composition according to claim 1 in which said calcium pyrophosphate is present in an amount of between 3% and 8%, preferably between 4.5% and 7.5 %, even more preferably between 5.5% and 7 %, by weight of the composition,

15 excluding any coating compositions.

3. The composition according to claim 1 formulated as a chewing gum composition in which said gum base constitutes from 10% to 99%, particularly from 15% to 80%, preferably 25% to 60 % by weight of the composition.

20

4. The composition according to claim 1 in which said gum base comprises one or more of the following; natural or synthetic elastomeric compounds, natural or synthetic resin compounds, fillers, softening compounds, antioxidants and colorants.

5. The composition according to claim 1 formulated as a confectionary composition in which said confectionary base constitutes from 0% to 99%, particularly from 15% to 98%, preferably 30% to 97% by weight of the composition.

5 6. The composition according to any of the preceding claims in which said conventional chewing gum or confectionary additives comprise one or more of the following ingredients: sweeteners, high intensity sweeteners, taste enhancers, flavouring agents, colouring agents.

10 7. The composition according to any of the preceding claims in which said composition is essentially sugar-free.

8. The composition according to any of the preceding claims comprising one or more additional tooth whitening agents.

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9. The composition according to claim 8 in which said additional tooth whitening agent(s) is/are present in between 0.01% and 10.0%, more particularly between 0.1 and 2.0%, preferably between 0.25% and 1.0% by weight of the composition, excluding any coating.

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10. The composition according to claim 8 or 9 in which said additional tooth whitening agent comprises a bicarbonate salt.

11. The composition according to claim 10 in which said additional tooth whitening

agent comprises sodium bicarbonate, said agent being present in between 0.3% and 0.4% by weight of the compositions excluding any coating.

12. The composition according to any of the preceding claims in which said additives and/or tooth whitening agents are encapsulated.

13. The composition according to any of the preceding claims further comprising one or more of the following: oral hygiene promoting agents, anti-calculus agents, anti-microbial agents, anti-inflammatory agents, desensitising agents, therapeutically active agents, remineralising agents.

14. The composition according to any of the preceding claims further comprising a supplement.

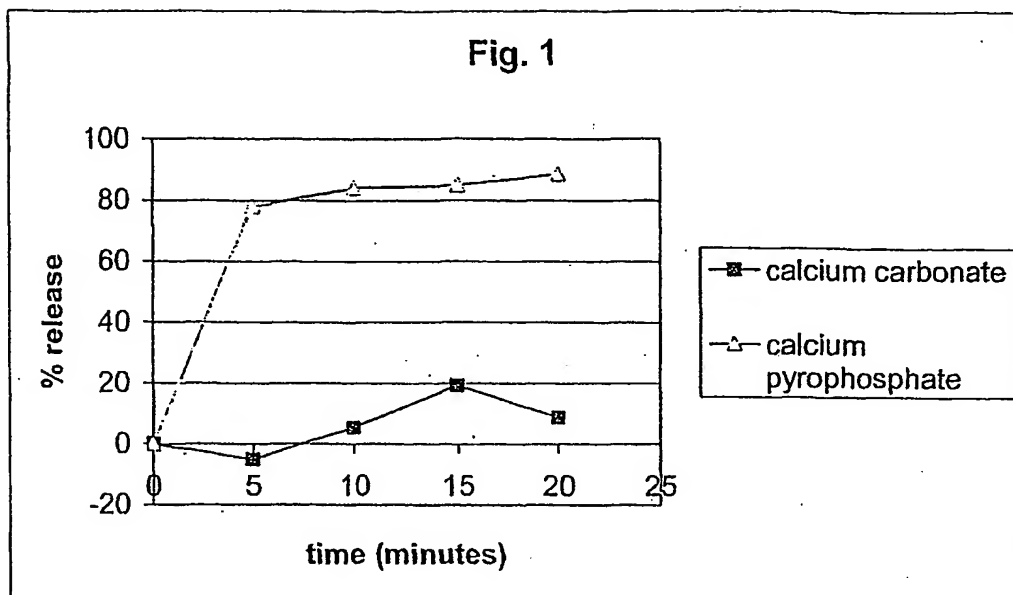
15. The composition according to claim 14 in which said supplement comprises vitamin C.

16. The composition according to claim 13 in which the oral hygiene promoting agent comprises urea, said urea being present in between 0.15% and 25%, particularly between 0.4% and 10%, preferably between 0.8% and 5%, even more preferably between 1.5 % and 2.5% by weight.

17. A use of a composition according to any of the preceding claims to whiten tooth surfaces.

18. A use of a composition according to claims 1-16 to whiten tooth surfaces, said tooth surfaces being discoloured after use of tobacco-related products.
- 5 19. A use of a composition according to any of the claims 1-16 to whiten tooth surfaces, said tooth surfaces being discoloured after use of coffee-related products.
20. A method of whitening tooth surfaces by consuming a solid, oral tooth whitening composition according to any of claims 1-16.
- 10 21. A method of whitening tooth surfaces by consuming a solid, oral tooth whitening composition according to claims 1-16, said tooth surfaces being discoloured after use of tobacco-related products.
- 15 22. A method of whitening tooth surfaces by consuming a solid, oral tooth whitening composition according to any of the claims 1-16, said tooth surfaces being discoloured after use of coffee-related products.

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP 03/13873

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 348 370 A (HODGES GERWYN TUDOR) 4 October 2000 (2000-10-04) the whole document	1-22
X	US 4 400 372 A (KLEBER CARL J ET AL) 23 August 1983 (1983-08-23) column 13, line 63 -column 14, line 14 column 17, line 23 -column 19, line 11 abstract	1-22
X	US 2003/072841 A1 (ERNST LISA CATRON ET AL) 17 April 2003 (2003-04-17) page 4, paragraph 38 page 7, paragraph 59 page 7, paragraph 63 page 8, paragraph 71 claims abstract	1-22
	-/--	

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PCT/EP 03/13873

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 897 548 A (KATZ SIMON) 29 July 1975 (1975-07-29) column 3, line 1 - line 20 column 6, line 6 - line 24; example 1 ---	1-22
X	WO 96 19190 A (HUGHES IAIN ALLAN ;PROCTER & GAMBLE (US)) 27 June 1996 (1996-06-27) page 7, paragraph 3 page 9, paragraph 3 page 10, paragraph 3 page 11, paragraph 3 claims abstract ---	1-22
X	US 6 355 229 B1 (ADAMY STEVEN T) 12 March 2002 (2002-03-12) column 4, line 10 - line 26; claims abstract ---	1-22
A	US 2003/099740 A1 (COLLE ROBERTO ET AL) 29 May 2003 (2003-05-29) claims abstract ---	12
A	EP 0 288 909 A (NABISCO BRANDS INC) 2 November 1988 (1988-11-02) abstract ---	12
A	US 3 957 967 A (L ORANGE PAUL) 18 May 1976 (1976-05-18) abstract ---	16
A	EP 0 236 290 A (MONSANTO CO) 9 September 1987 (1987-09-09) abstract -----	1-22

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No

PCT/EP 03/13873

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 2348370	A	04-10-2000	NONE	
US 4400372	A	23-08-1983	AT 13809 T	15-07-1985
			AU 549059 B2	09-01-1986
			AU 8106882 A	09-09-1982
			CA 1188619 A1	11-06-1985
			DE 3264189 D1	25-07-1985
			EP 0060088 A2	15-09-1982
			NZ 199872 A	14-12-1984
			JP 1557254 C	16-05-1990
			JP 57208954 A	22-12-1982
			JP 63066498 B	21-12-1988
US 2003072841	A1	17-04-2003	CA 2441536 A1	26-09-2002
			EP 1370152 A2	17-12-2003
			HU 0303471 A2	01-03-2004
			WO 02074099 A2	26-09-2002
			CA 2441865 A1	26-09-2002
			EP 1370227 A2	17-12-2003
			HU 0303498 A2	01-03-2004
			WO 02074274 A2	26-09-2002
			WO 02074276 A2	26-09-2002
			US 2002187108 A1	12-12-2002
			US 6500406 B1	31-12-2002
			US 2003086878 A1	08-05-2003
			US 2003082113 A1	01-05-2003
US 3897548	A	29-07-1975	BE 813420 A1	08-10-1974
			CA 1029308 A1	11-04-1978
			DE 2416542 A1	24-10-1974
			FR 2224162 A1	31-10-1974
			GB 1453532 A	27-10-1976
			JP 50069242 A	10-06-1975
			NL 7404742 A	11-10-1974
WO 9619190	A	27-06-1996	AU 688185 B2	05-03-1998
			AU 4241896 A	10-07-1996
			BR 9510483 A	02-06-1998
			CA 2208442 A1	27-06-1996
			CN 1170351 A ,B	14-01-1998
			CZ 9701883 A3	12-11-1997
			EP 0801555 A1	22-10-1997
			HU 77712 A2	28-07-1998
			JP 10511092 T	27-10-1998
			KR 246833 B1	01-04-2000
			NZ 297291 A	29-03-1999
			PL 320869 A1	10-11-1997
			SK 83497 A3	14-01-1998
			TR 960606 A2	21-07-1996
			WO 9619190 A1	27-06-1996
			US 6294154 B1	25-09-2001
US 6355229	B1	12-03-2002	WO 03002056 A2	09-01-2003
US 2003099740	A1	29-05-2003	IT T020000394 A1	26-10-2001
			AU 3739501 A	07-11-2001
			BR 0106275 A	19-03-2002
			CA 2377185 A1	01-11-2001

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP 03/13873

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 2003099740	A1		CN 1366451 T	28-08-2002
			CZ 20020223 A3	17-04-2002
			WO 0180661 A1	01-11-2001
			EP 1276386 A1	22-01-2003
			HU 0202859 A2	28-12-2002
			JP 2003530865 T	21-10-2003
			PL 351400 A1	07-04-2003

EP 0288909	A	02-11-1988	US 4975270 A	04-12-1990
			AU 1517688 A	27-10-1988
			CA 1336750 C	22-08-1995
			EP 0288909 A1	02-11-1988
			ZA 8802819 A	20-10-1988

US 3957967	A	18-05-1976	DE 2338177 A1	17-04-1975
			CA 1034505 A1	11-07-1978
			FR 2238475 A1	21-02-1975
			GB 1483726 A	24-08-1977
			IT 1049201 B	20-01-1981
			JP 50069243 A	10-06-1975

EP 0236290	A	09-09-1987	AU 6966587 A	10-09-1987
			EP 0236290 A1	09-09-1987
			PT 84397 A ,B	01-04-1987

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